This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 21

See attached form for additional information.

Interagency Report Control No.:

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. CERTIFICATE NUMBER: 23-R-0033
CUSTOMER NUMBER: 337

FORM APPROVED
OMB NO. 0579-0036

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

Childrens Hospital Of Philadelphia
Joseph Stokes Jr Res Inst
3516 Civic Center Blvd.
Philadelphia, PA 19104

NOV 15 2005

Telephone: (215) -590-3800

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, or experimentation, or held for these purposes. Attach additional sheets if necessary)

FACILITY LOCATIONS (Sites) - See Atached Listing

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY **(Attach additional sheets if necessarv or use APHIS Form 7023A)**

A. Animals Covered By The Animal Welfare Regulations	B. Number of animal being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not ye used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use o pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals an for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for wh the use of appropriate anesthetic, analgesic, or tranquiliz drugs would have adversely affected the procedures, res or interpretation of the teaching, research, experiments, surgery, or tests. (An explanation of the procedures producing pain or distress in these animals and the reasc such drugs were not used must be attached to this report	F. TOTAL NUMBER OF ANIMALS (COLUMNS C + D + E)
4. Dogs	0	0	0	0	0
5. Cats	0	0	0	0	0
6. Guinea Pigs	0	0	0	0	0
7. Hamsters	0	0	0	0	0
8. Rabbits	0	54	91	0	145
9. Non-human Primates	0	0	0	0	0
10. Sheep	0	5	2	0	7
11. Pigs	0	32	109	0	141
12. Other Farm Animals					
13. Other Animals					

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anestetic, analgesic, and tranquilizing drugs, prior to, during, and following actual rese teaching, testing, surgery, or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and ap Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary inc brief explanation of the exceptions, as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional Official)

SIGNATURE OF C.E.O. OR INSTITUTIONAL OFFICIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL *(Type or Print)*	DATE SIGNED
[redacted]	(b)(6), (b)(7)c	11/9/05

APHIS FORM 7
(AUG 91)

Registration #23-R-0033

NOV 15 2005

The IACUC has approved protocols that require multiple survival surgeries:

Procedure for monitoring these activities:
All multiple major survival surgery protocols in large animals are monitored by the Veterinary Technicians who ensure that all records on these animals are maintained in the Laboratory Animal Facility (LAF). These individuals check on all of the animals every day in the LAF. All LAF staff monitor animals during the course of their daily activities and any animals in need of care are brought to the attention of the Attending Veterinarian and/or the Veterinary Technicians. Monitoring plans are developed on a protocol-by-protocol basis.

Protocols approved for multiple survival surgeries:

a) A protocol is approved to evaluate the effects of correction of partial bladder obstruction in rabbits (03-289). In the first surgery, a suture is placed around the urethra while a catheter is in place. Between two and ten weeks later, a second midline incision is performed and the suture that restricts the urethra is removed and a small biopsy of the bladder is performed. Animals are then monitored for voiding patterns and/or sacrificed for analyses of molecular correlates of recovery.

b) A protocol to develop an animal model of spina bifida and evaluate strategies for in utero correction is approved in sheep (04-414). At 75 days gestation, a surgical procedure is performed to create the myelomeningocoele defect (spina bifida). At 100 days gestation, a second surgical procedure is performed to correct the defect in some of the animals. At 135-138 days gestation, the animals are delivered by caesarean section. After up to three days, the lambs are euthanized and tissues are harvested for evaluation.

c) A protocol is approved to determine if growth factor expression from an adenoviral vector facilitates wound healing and prevents scar formation (02-451). In this protocol, a small (2 x 2 mm) wound to the cricoid is performed in an adult rabbit. Two weeks later the incision is reopened and an adenoviral vector that should expresses TGFß3 applied to the wound site. After up to three weeks, the animal is euthanized for analysis of healing and transgene expression. **This protocol was terminated by the investigator on 6/2/05.**

d) A protocol is approved to repeatedly harvest oocytes from xenopus (03-470). The investigator is approved to remove oocytes up to five total times from xenopus with at least one-month wait between each surgical procedure.

e) A protocol is approved to study techniques to determine if it is possible to maintain/lengthen blood vessels in culture and then implant them back into the same pig to determine if the vessels are viable (03-490). In the first surgery a segment of the carotid artery is replaced with a segment of the saphenous vein. After maintaining the carotid artery in culture for nine days, it is replaced back into the animal. The patency of the vessel is assessed using a Doppler flow probe two weeks later, and then the animal is euthanized in a terminal surgical procedure after one month to harvest and evaluate the grafts. **This protocol was terminated by the investigator on 7/19/05.**

f) A protocol is approved to create a left-sided diaphragmatic hernia in fetal sheep at approximately 65 days of gestation and determine if tracheal occlusion combined with maternal administration of glucocorticoids can be used to correct the defect (02-616). At approximately 110 days of gestation, the trachea on the same animal is occluded. At 138-140 days of gestation, the lambs are partially delivered by C-section. After a series of blood flow and pulmonary function tests lasting approximately two hours, the lamb is euthanized. **This protocol was terminated by the investigator on 7/5/05.**

g) A protocol is approved to study the effects of tracheal occlusion for the treatment of the effects of diaphragmatic hernia using a fetal sheep model (03-652). At approximately 65 days of gestation, a left-sided diaphragmatic hernia is created. At approximately 110 days of gestation, a tracheal occlusion is performed and at 130 days gestation the tracheal occlusion is released. At approximately 138-140 days gestation, the lambs are partially delivered. A series of tests of fluid absorption are made and within three hours the lambs and the ewes are euthanized. **This protocol was terminated by the investigator on 7/5/05.**

h) A protocol is approved to study pulmonary hypertension observed in a sheep model of congenital diaphragmatic hernia (03-653). At approximately 65 days of gestation, a left-sided diaphragmatic hernia is created. At approximately 139 days of gestation, the lamb is delivered by C-section and the ewe with any unmanipulated lambs are euthanized. The lamb with the surgically introduced diaphragmatic hernia is kept continuously sedated and the responsiveness of the pulmonary system to pharmacologic agents is evaluated. (This is reported as multiple survival surgeries because the fetus undergoes two manipulations). **This protocol was terminated by the investigator on 7/5/05.**

i) A protocol is approved to study in utero bone marrow transplantation and postnatal engraftment enhancement techniques in a canine model (05-707). At gestational day 37, fetuses will undergo in utero bone marrow transplant. At between one and six months of age, some of these animals will undergo skin grafting to assess immune tolerance. In a different aim, similar studies will involve bone marrow transplant at gestational day 37, and at between one and six months of age these animals will receive a second bone marrow transplant. The IACUC also approved performing the in utero bone marrow transplant as described above and performing a C-section if it were medically required to protect the bitch or the fetus.

j) A protocol is approved to establish an in vivo model of subglottic stenosis that minimizes pain, suffering and respiratory compromise and to determine the effects of cytokine manipulation on subglottic scarring in a rabbit model (04-717). A section of the trachea will be transferred to a subcutaneous pocket. Four weeks after the engraftment, a small incision will be made and the tracheal tissue will be evaluated with an endoscope and in some animals the tissue will be injured. One week later a small incision will be made and the injured tissue will be treated with an adenoviral vector encoding a potentially therapeutic gene, a control vector, or vehicle. Six weeks later the tracheal transplant will be evaluated by endoscopy in a terminal anesthetic procedure and the tissue harvested for histopathologic evaluation.

Addendum **Registration #23-R-0033**

Food or Fluid Restriction

Experimental situations that require food and/or fluid restriction:

Title of Experiment	Justification	Species	Length of Restriction
1. Functional Outcomes of Myelomeningocoele Repairs in Utero (01-414) 2. Cardiac Valvuloplasty in Fetal Sheep (02-604) 3. Tracheal Occlusion for Diaphragmatic Hernia (02-616) * 4. Lung Liquid Reabsorption Following Prenatal Tracheal Occlusion (03-652) * 5. Manipulation of Pulmonary Vascular Resistance in Congenital Diaphragmatic Hernia (03-653) * 6. Fetal Cardiac Therapy (04-697) ** 7. Pharmacological Treatment of Pulmonary Hypertension (05-741)	Prevention of vomiting and aspiration of stomach contents during anesthetic induction of pregnant sheep.	Sheep	Food withheld for 48 hours prior to surgery with unrestricted access to water.

* **Terminated by investigator on 7/5/05.**
** **Terminated by investigator on 4/21/05.**

→ **Number of Sheep Affected for this Reporting Period: 7**
(1 was fasted for 24 hours; 6 were fasted for 48 hours)

Variables that are monitored to ensure animal health during the restricted period.
When sheep are fasted for 48 hours, a form is placed on the cage where urine/fecal output is noted daily. If a decrease in fecal or urine output is noted, a Veterinary Technician is notified.

Steps taken to ensure adequate nutrition/hydration during the restricted period.
The sheep are allowed free access to water at all times. We have not observed detrimental effects in the sheep from food restriction, and have a low rate of complications with survival sheep fetal surgeries.

Addendum **Registration #23-R-0033**

The IACUC has approved two exceptions on animal space provisions:

1. The size of cages for sheep is slightly less (18 sq. ft.) than the size identified in the Guide (20 sq. ft.). This decision was based on the recommendation of the Attending Veterinarian and the LAF Manager. These individuals had polled other institutions who indicated that, in their experience, sheep are able to stand, turn around, and lie down in this size cage. The cage size was adopted by the IACUC at its' May 12, 1997 meeting. Since we adopted the use of this size cage, we have observed no evidence of unusual or abnormal behaviors associated with this cage.

   → **Number of Sheep Affected for this Reporting Period: 7**

2. A subcommittee of the IACUC met on December 2, 2002 to observe swine that were larger than 100 kg, but smaller than 200 kg in weight. These animals were being housed in 24 sq. ft. of space. The Guide calls for 24 sq. ft. for 100 kg swine and 48 sq. ft. for up to 200 kg swine. The subcommittee recommended that swine up to 200 kg in weight could be housed in 24 sq. ft. because they were able to stand around and lie down in apparent comfort. The cage size was adopted by the IACUC at its' December 9, 2002 meeting. Since we adopted the use of this size cage, we have observed no evidence of unusual or abnormal behaviors associated with this cage.

   → **Number of Swine Affected for this Reporting Period: 0**